Photonic inspection of cardiac myocyte cell contractions

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A lensless optical configuration comprising laser and camera provides an ‘instant snapshot’ of the contraction statistics of muscle cells in an illuminated culture.

Cardiovascular disease is America’s number one killer, accounting for more than 41% of deaths each year. Furthermore, 61 million Americans have some form of the condition, including heart disease, stroke, high blood pressure, congestive heart failure, congenital heart defects, and hardening of the arteries. Early detection of abnormality is the key to treating cardiovascular disease and reducing the death toll. However, some conditions, such as myocardial ischemia (reduced blood supply to the heart), can be difficult to establish in the early stages, which is when treatment is most effective.

Cardiac ischemia is currently diagnosed by measuring electrical signals from the heart, or by using ultrasound waves to analyze heart contractions. Our study aims to understand the contraction behavior of cardiac myocytes (muscle cells) in their simplest form: in a culture. We propose a robust way to test the influence of certain substances on the rate and magnitude of those contractions. Our work enables precise measurement (with nanometer accuracy) of the propagation of electronic stimulation waves within the culture. Such capability could be useful for studying re-entrant arrhythmias, when the electrical signal travels in a circle, instead of propagating in a linear fashion. Re-entrant arrhythmias can be detected on the pericardium (outer wall) of the heart.

We propose a very simple configuration to assess the statistics of cell contractions by measuring their physical contraction and expansion following illumination and analysis of the resulting secondary speckle patterns. Our system provides an ‘instant snapshot’ of the sample, enabling the study of numerous cells, and obtains statistics of their contractions.

We illuminate the culture with a laser, while a camera positioned at a given distance from the culture collects the back-reflected light, which interacts with the myocyte cells. The light generates a secondary speckle pattern on the detection plane array of the camera, and we can sample and analyze temporal changes in that pattern.

Our method yields good results without using any imaging lenses, and is therefore a simple and inexpensive way to extract the cells’ contraction statistics. It also provides a rough estimate of the spatial distribution of the cells within the inspected culture by positioning the lensless camera a few millimeters away. We track the movement of the generated secondary speckle pattern using correlation-based algorithms, and from this translate the movement of the speckle to the movement of the cells themselves. Taking into account the distance of the optical system from the culture, and by carefully adjusting the algorithms, we can extract 3D movement of the contraction profile with nanometric accuracy.

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Figure 1 shows experimental results we obtained. The experiment was performed on cultured 4–6-day-old rat cardiac myocytes. We applied an electrical signal using a Grass SD9 stimulator. The signals had a frequency of 1Hz, a pulse width of 10ms, and an amplitude of 50V. The laser was a PhotopDPGL-2050F with a typical wavelength of 532nm and optical output power of 50mW. We captured the reflected speckles from the cells directly by a PixeLink camera with a CMOS detector and 5.2 × 5.2μm pixel size. We analyzed the recorded data using a Matlab script. The figure clearly shows a 30-frame gap between two adjacent peaks, indicating the 1Hz stimulus and 30-frames-per-second sampling rate. The novelty of the result is that a simple and lensless configuration can be used for simultaneously obtaining statistically averaged information about the contraction of a large number of cells (all the cells that are illuminated by the laser beam, which in our case was around 1000 cells).

Our proposed configuration could be useful for evaluating the effect of new drugs, for example, isoproteranol, a medication to treat slow heart rate. In future work, we plan to develop a microfluidic chip (one that manipulates very small quantities of fluids) that incorporates our lensless concept in a compact diagnostic device. The technology could be used to investigate myocyte cells in relation to other cardiovascular conditions, such as reciprocal or echo beats, or reciprocating tachycardia.

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